

ASYMPTOTIC PROFILES OF THE STEADY STATES FOR AN SIS EPIDEMIC PATCH MODEL*

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Abstract. Spatial heterogeneity, habitat connectivity, and rates of movement can have large impacts on the persistence and extinction of infectious diseases. These factors are shown to determine the asymptotic profile of the steady states in a frequency-dependent SIS (susceptible-infected-susceptible) epidemic model with n patches in which susceptible and infected individuals can both move between patches. Patch differences in local disease transmission and recovery rates characterize whether patches are low-risk or high-risk, and these differences collectively determine whether the spatial domain, or habitat, is low-risk or high-risk. The basic reproduction number \mathcal{R}_0 for the model is determined. It is then shown that when the disease-free equilibrium is stable ($\mathcal{R}_0 < 1$) it is globally asymptotically stable, and that when the disease-free equilibrium is unstable ($\mathcal{R}_0 > 1$) there exists a unique endemic equilibrium. Two main theorems link spatial heterogeneity, habitat connectivity, and rates of movement to disease persistence and extinction. The first theorem relates the basic reproduction number to the heterogeneity of the spatial domain. For low-risk domains, the disease-free equilibrium is stable ($\mathcal{R}_0 < 1$) if and only if the mobility of infected individuals lies above a threshold value, but for high-risk domains, the disease-free equilibrium is always unstable ($\mathcal{R}_0 > 1$). The second theorem states that when the endemic equilibrium exists, it tends to a spatially inhomogeneous disease-free equilibrium as the mobility of susceptible individuals tends to zero. This limiting disease-free equilibrium has a positive number of susceptible individuals on all low-risk patches and can also have a positive number of susceptible individuals on some, but not all, high-risk patches. Sufficient conditions for whether high-risk patches in the limiting disease-free equilibrium have susceptible individuals or not are given in terms of habitat connectivity, and these conditions are illustrated using numerical examples. These results have important implications for disease control.

Key words. spatial heterogeneity, dispersal, habitat connectivity, basic reproduction number, disease-free equilibrium, endemic equilibrium

AMS subject classifications. 92D30, 92D40, 92D50, 91D25, 34C60, 37N25

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1. Introduction. Spatial heterogeneity, habitat connectivity, and rates of movement play important roles in disease persistence and extinction. Movement of susceptible or infected individuals can enhance or suppress the spread of disease, depending on the heterogeneity and connectivity of the spatial environment (see, e.g., Castillo-Chavez and Yakubu (2001, 2002); Bolker and Grenfell (1995); Hess (1996); Lloyd and May (2001); Salmani and van den Driessche (2006); Ruan (2006); Allen et al. (2007)). For example, the compartmental patch model of Ruan, Wang, and

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Levin (2006) demonstrates that diseases such as SARS can be contained by screening for infection at borders and barring residents of disease hot spots from travel. Spatial heterogeneity can also give rise to complex and surprising disease dynamics (Allen, Kirupaharan, and Wilson (2004); Castillo-Chavez and Yakubu (2001, 2002); Hess (1996); Lloyd and Jansen (2004); Wang and Zhao (2004)). In numerical investigations of a discrete-time two-patch SIS (susceptible-infected-susceptible) epidemic model, Allen, Kirupaharan, and Wilson (2004) considered a case where, in the absence of movement, the disease persists in only one of the two patches—a high-risk patch, where the patch reproduction number is greater than one. When the patches are connected by susceptible and infective movement, an endemic equilibrium is reached in both patches. But if the movement pattern is changed so that only infected individuals disperse between the two patches, a surprising result occurs. The disease does not persist in either patch; the high-risk patch becomes empty, and all susceptible individuals eventually reside in the low-risk patch, where the patch reproduction number is less than one. We investigate this latter phenomenon in a continuous-time SIS metapopulation model with n patches that includes both high-risk and low-risk patches.

Disease spread in metapopulation models involving discrete patches has been investigated in a variety of settings (Arino and van den Driessche (2006, 2003a, 2003b); Arino et al. (2005); Jin and Wang (2005); Rvachev and Longini (1985); Salmani and van den Driessche (2006); Sattenspiel and Dietz (1995); Wang and Mulone (2003); Wang and Zhao (2004)). In a review article, Arino and van den Driessche (2006) summarize some known results on disease dynamics in metapopulation models with regard to existence and stability of disease-free and endemic equilibria. They develop a general framework for movement of susceptible, exposed, infected, and recovered individuals (SEIRS model) and define a *mobility matrix*, an irreducible matrix that defines the spatial arrangement of patches and rates of movement between patches (see also Arino and van den Driessche (2003a, 2003b)). Wang and colleagues studied uniform persistence and global stability of disease-free and endemic equilibria in SIS metapopulation models (Jin and Wang (2005); Wang and Mulone (2003); Wang and Zhao (2004)).

Here, we formulate a frequency-dependent SIS metapopulation model consisting of n patches. The spatial arrangement of patches, and rates of movement between patches, are defined by an irreducible matrix. The spatial domain is characterized as *low-risk* or *high-risk* if the spatial average of the patch transmission rates is less than or greater than, respectively, the spatial average of the recovery rates. Individual patches are also characterized as *low-risk* or *high-risk* if the patch transmission rate is less than or greater than the patch recovery rate, which is equivalent to the patch reproduction number being less than or greater than one, respectively. A unique disease-free equilibrium is shown to exist, and a basic reproduction number \mathcal{R}_0 is determined. If $\mathcal{R}_0 < 1$, the disease-free equilibrium is shown to be globally asymptotically stable, and if $\mathcal{R}_0 > 1$, a unique endemic equilibrium is shown to exist.

Our two main theorems link spatial heterogeneity, habitat connectivity, and rates of movement to disease persistence and extinction. The first theorem relates the basic reproduction number to the heterogeneity of the spatial domain. It is shown that for low-risk domains, the disease-free equilibrium is stable ($\mathcal{R}_0 < 1$) if and only if the mobility of infected individuals lies above a threshold value. For high-risk domains the disease-free equilibrium is always unstable ($\mathcal{R}_0 > 1$). The second theorem concerns the spatial heterogeneity in the limiting case where the mobility of susceptible individuals approaches zero. We show that if $\mathcal{R}_0 > 1$, then the endemic

equilibrium approaches a spatially inhomogeneous disease-free equilibrium which has a positive number of susceptible individuals on all low-risk patches and no susceptibles on at least one of the high-risk patches. These results have important implications for disease control. If the spatial environment can be modified to include low-risk patches (i.e., low transmission rates or high recovery rates) and if the movement of susceptible individuals can be restricted (e.g., quarantine), then it may be possible to eliminate the disease.

1.1. The model. Let $n \geq 2$ be the number of patches and $\Omega = \{1, 2, \dots, n\}$. Consider the SIS patch model

$$(1.1a) \quad \frac{d\bar{S}_j}{dt} = d_S \sum_{k \in \Omega} (L_{jk}\bar{S}_k - L_{kj}\bar{S}_j) - \frac{\beta_j \bar{S}_j \bar{I}_j}{\bar{S}_j + \bar{I}_j} + \gamma_j \bar{I}_j, \quad j \in \Omega,$$

$$(1.1b) \quad \frac{d\bar{I}_j}{dt} = d_I \sum_{k \in \Omega} (L_{jk}\bar{I}_k - L_{kj}\bar{I}_j) + \frac{\beta_j \bar{S}_j \bar{I}_j}{\bar{S}_j + \bar{I}_j} - \gamma_j \bar{I}_j, \quad j \in \Omega,$$

where $\bar{S}_j(t)$ and $\bar{I}_j(t)$ denote the number of susceptible and infected individuals in patch j at time $t \geq 0$; d_S and d_I are positive diffusion coefficients for the susceptible and infected subpopulations; L_{jk} represents the degree of movement from patch k into patch j ; and β_j and γ_j are nonnegative constants that express the rate of disease transmission and recovery in patch j . Because $\bar{S}_j \bar{I}_j / (\bar{S}_j + \bar{I}_j)$ is a Lipschitz continuous function of \bar{S}_j and \bar{I}_j in the open first quadrant, we extend its definition to the entire first quadrant by defining it to be zero when at least one of $\bar{S}_j = 0$ or $\bar{I}_j = 0$ holds. We assume that

$$(A1) \quad \bar{S}_j(0) \geq 0 \text{ and } \bar{I}_j(0) \geq 0 \text{ for } j \in \Omega, \text{ and } \sum_{j \in \Omega} [\bar{S}_j(0) + \bar{I}_j(0)] > 0.$$

Let $\bar{S} = (\bar{S}_j)$ and $\bar{I} = (\bar{I}_j)$. Brauer and Nohel's work (1989) implies that a unique solution (\bar{S}, \bar{I}) of (1.1) exists for all time. Let

$$(1.2) \quad N = \sum_{j \in \Omega} [\bar{S}_j(0) + \bar{I}_j(0)]$$

be the total number of individuals in all patches at $t = 0$. By (A1), N is positive. Summing the $2n$ equations in (1.1) makes it clear that

$$(1.3) \quad \sum_{j \in \Omega} [\bar{S}_j(t) + \bar{I}_j(t)] = N, \quad t \geq 0.$$

We will assume that the *connectivity matrix* $L = (L_{jk})$ satisfies

$$(A2) \quad L \text{ is nonnegative, irreducible, and symmetric.}$$

We shall say that a matrix $A = (A_{jk})$ is *nonnegative* (or *positive*) if all its elements are nonnegative (or positive), in which case we will write $A \geq 0$ (or $A > 0$). Similar comments apply to vectors $u = (u_j)$. The symmetry assumption ensures that the per capita rates of susceptible and infected individuals entering patch j from patch k ($d_S L_{jk}$ and $d_I L_{jk}$) are equal to the per capita rates of individuals moving in the other direction ($d_S L_{kj}$ and $d_I L_{kj}$). Hence, in (1.1)

$$L_{jk}\bar{S}_k - L_{kj}\bar{S}_j = L_{jk}(\bar{S}_k - \bar{S}_j) \quad \text{and} \quad L_{jk}\bar{I}_k - L_{kj}\bar{I}_j = L_{jk}(\bar{I}_k - \bar{I}_j).$$

The irreducibility assumption implies that the system of patches considered as a directed graph with patches as the vertices is strongly connected (Ortega (1987)).

Other characterizations of irreducibility are given in Appendix A, and we will make use of these additional facts as needed.

We say that in a *low-risk patch* disease transmission occurs at a lower rate than disease recovery when the number of infected individuals in that patch is very small. A *high-risk patch* is defined in a similar manner. Let

$$H^- = \{j \in \Omega : \beta_j < \gamma_j\} \quad \text{and} \quad H^+ = \{j \in \Omega : \beta_j > \gamma_j\}$$

denote the set of these low-risk and high-risk patches, respectively. We assume that

$$(A3) \quad H^- \text{ and } H^+ \text{ are nonempty and } H^- \cup H^+ = \Omega.$$

Let $\mathcal{R}_0^{[j]} = \beta_j/\gamma_j$ be the *patch reproduction number* for patch $j \in \Omega$ (we set $\mathcal{R}_0^{[j]} = \infty$ when $\gamma_j = 0$). Then $\mathcal{R}_0^{[j]} < 1$ for low-risk patches ($j \in H^-$), and $\mathcal{R}_0^{[j]} > 1$ for high-risk patches ($j \in H^+$). It is well known that the disease can persist in isolated high-risk patches but not in isolated low-risk patches.

Let

$$\Sigma_\beta = \sum_{j \in \Omega} \beta_j \quad \text{and} \quad \Sigma_\gamma = \sum_{j \in \Omega} \gamma_j.$$

We say that Ω is a *low-risk domain* if $\Sigma_\beta < \Sigma_\gamma$, but a *high-risk domain* if $\Sigma_\beta \geq \Sigma_\gamma$.

For an arbitrary patch $j \in \Omega$, it will be convenient to define

$$L_j = \sum_{k \in \Omega} L_{jk}, \quad L_j^- = \sum_{k \in H^-} L_{jk}, \quad \text{and} \quad L_j^+ = \sum_{k \in H^+} L_{jk}.$$

These sums denote the connectivity between patch j and all patches, all low-risk patches, and all high-risk patches, respectively. The irreducibility of L implies that $L_j > 0$ for all $j \in \Omega$.

1.2. The equilibrium problem. We will be primarily interested in equilibrium solutions of (1.1), i.e., solutions of

$$(1.4a) \quad d_S \sum_{k \in \Omega} L_{jk} (\tilde{S}_k - \tilde{S}_j) - \frac{\beta_j \tilde{S}_j \tilde{I}_j}{\tilde{S}_j + \tilde{I}_j} + \gamma_j \tilde{I}_j = 0, \quad j \in \Omega,$$

$$(1.4b) \quad d_I \sum_{k \in \Omega} L_{jk} (\tilde{I}_k - \tilde{I}_j) + \frac{\beta_j \tilde{S}_j \tilde{I}_j}{\tilde{S}_j + \tilde{I}_j} - \gamma_j \tilde{I}_j = 0, \quad j \in \Omega,$$

where \tilde{S}_j and \tilde{I}_j denote the number of susceptible and infected individuals, respectively, in patch $j \in \Omega$ at equilibrium. In view of (1.3), we impose the condition

$$(1.4c) \quad \sum_{j \in \Omega} (\tilde{S}_j + \tilde{I}_j) = N.$$

Let $\tilde{S} = (\tilde{S}_j)$ and $\tilde{I} = (\tilde{I}_j)$. We are interested only in solutions (\tilde{S}, \tilde{I}) of (1.4) which satisfy $\tilde{S} \geq 0$ and $\tilde{I} \geq 0$. A *disease-free equilibrium* (DFE) is a solution in which $\tilde{I}_j = 0$ for all $j \in \Omega$. An *endemic equilibrium* (EE) is a solution in which $\tilde{I}_j > 0$ for some $j \in \Omega$. To distinguish between these two types of equilibria, we will for notational convenience denote a DFE by $(\hat{S}, 0)$ and an EE by (\tilde{S}, \tilde{I}) .

1.3. Statement of the main results. We consider in section 2 properties of the DFE, including its existence, uniqueness, and stability. We first show that there exists a unique DFE $(\hat{S}, 0)$, and it is given by $\hat{S}_j = N/n$ for $j \in \Omega$. We then calculate the basic reproduction number \mathcal{R}_0 for (1.1) using the next generation approach (Diekmann, Heesterbeek, and Metz (1990), Diekmann and Heesterbeek (2000), van den Driessche and Watmough (2002)) for which it is known that if $\mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable, but if $\mathcal{R}_0 > 1$, then it is unstable. Our calculation will show that \mathcal{R}_0 does not depend on the diffusion coefficient d_S . Finally, we show that if $\mathcal{R}_0 < 1$, then the DFE is globally asymptotically stable.

In section 3, we find an equivalent characterization for the stability of the DFE in terms of d_I rather than \mathcal{R}_0 . In particular, we show that the DFE in a low-risk domain is stable if and only if the diffusion coefficient for infected individuals lies above a certain threshold value, but in a high-risk domain, the DFE is always unstable. We also show that when the DFE is unstable, then there exists a unique EE. Moreover, the disease persists in every patch.

THEOREM 1. *Suppose that (A1)–(A3) hold and N is fixed.*

- (a) *In a low-risk domain ($\Sigma_\beta < \Sigma_\gamma$), there exists a threshold value $d_I^* \in (0, \infty)$ such that $\mathcal{R}_0 > 1$ for $d_I < d_I^*$ and $\mathcal{R}_0 < 1$ for $d_I > d_I^*$.*
- (b) *In a high-risk domain ($\Sigma_\beta \geq \Sigma_\gamma$), we have $\mathcal{R}_0 > 1$ for all d_I .*
- (c) *If $\mathcal{R}_0 > 1$, then an EE exists, it is unique, and $\tilde{I} > 0$.*

Observe from (1.4) that in the limiting case $d_S = 0$ there also exists a family of infinitely many spatially inhomogeneous DFEs $(\hat{S}, 0)$, each of which satisfies

$$(1.5) \quad \hat{S} \geq 0 \quad \text{and} \quad \sum_{j \in \Omega} \hat{S}_j = N.$$

In section 4, we show that if $\mathcal{R}_0 > 1$, then the EE approaches such a spatially inhomogeneous DFE as the mobility of susceptible individuals becomes very small. We write this limiting DFE as $(S^*, 0)$ and also consider the distribution of patches for which S^* is either positive or zero.

THEOREM 2. *Suppose that (A1)–(A3) hold, N is fixed, and $\mathcal{R}_0 > 1$.*

- (a) *$(\tilde{S}, \tilde{I}) \rightarrow (S^*, 0)$ as $d_S \rightarrow 0$ for some S^* satisfying (1.5);*
- (b) *$S^* > 0$ on H^- and $S_j^* = 0$ for some $j \in H^+$;*
- (c) *if*

$$(1.6) \quad \frac{1}{d_I} > \max_{k \in H^+} \left[\frac{L_k^-}{\beta_k - \gamma_k} \right] + \max_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right],$$

then $S^ \equiv 0$ on H^+ ;*

- (d) *if*

$$(1.7) \quad \frac{1}{d_I} < \frac{L_j^-}{\beta_j - \gamma_j} + \min_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right]$$

for some $j \in H^+$, then $S_j^ > 0$.*

We now make several remarks concerning Theorem 2, which connects spatial heterogeneity, habitat connectivity, and rates of movement. First, condition (1.6) will be satisfied whenever d_I is sufficiently small.

Second, Theorem 2(c) immediately implies that if

$$(1.8) \quad \frac{1}{d_I} > \max_{k \in H^+} \left[\frac{L_k^-}{\beta_k - \gamma_k} \right],$$

then $S^* \equiv 0$ on H^+ because $L_k^+ / (\beta_k - \gamma_k)$ is nonpositive for every $k \in H^-$. Although condition (1.6) is more inclusive than condition (1.8), the latter is usually easier to verify. Furthermore, if some low-risk patch ($k \in H^-$) is not directly connected to any high-risk patches ($L_k^+ = 0$), then conditions (1.6) and (1.8) are in fact equivalent.

Third, Theorem 2(d) implies that if

$$(1.9) \quad \frac{1}{d_I} < \max_{k \in H^+} \left[\frac{L_k^-}{\beta_k - \gamma_k} \right] + \min_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right],$$

then $S^* \neq 0$ on H^+ .

1.4. Examples. Before proving Theorems 1 and 2, we first illustrate the second theorem with some examples of metapopulations occupying different distributions of low-risk and high-risk patches.

Example 1. If $H^- = \{1, 2, \dots, n-1\}$ and $H^+ = \{n\}$, then Theorem 2(b) implies that $S^* > 0$ on H^- and $S^* = 0$ on H^+ . For this case, condition (1.6) in Theorem 2(c) may or may not hold, but condition (1.7) in Theorem 2(d) cannot. That is, for this particular configuration of patches, the assumption that $\mathcal{R}_0 > 1$ in Theorem 2 excludes the possibility that condition (1.7) can be satisfied.

Example 2. If $H^- = \{1\}$ and $H^+ = \{2, 3, \dots, n\}$, then

$$\max_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right] = \min_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right] = \frac{L_1^+}{\beta_1 - \gamma_1}.$$

Theorem 2(b) implies that $S^* > 0$ on H^- , and Theorem 2(c), (d) provide necessary and sufficient conditions (except in the case of equality) for determining whether $S^* \equiv 0$ or $S^* \neq 0$ on H^+ . For example, suppose that there are $n = 3$ patches with $H^- = \{1\}$ and $H^+ = \{2, 3\}$. If

$$\frac{1}{d_I} > \max \left\{ \frac{L_{21}}{\beta_2 - \gamma_2}, \frac{L_{31}}{\beta_3 - \gamma_3} \right\} + \frac{L_{12} + L_{13}}{\beta_1 - \gamma_1},$$

then $S^* \equiv 0$ on H^+ , but if

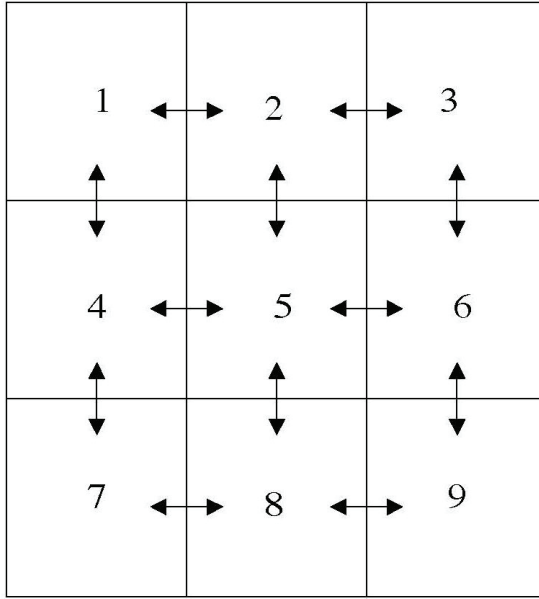
$$\frac{1}{d_I} < \max \left\{ \frac{L_{21}}{\beta_2 - \gamma_2}, \frac{L_{31}}{\beta_3 - \gamma_3} \right\} + \frac{L_{12} + L_{13}}{\beta_1 - \gamma_1},$$

then either $S_2^* = 0$ and $S_3^* > 0$ or $S_2^* > 0$ and $S_3^* = 0$.

Example 3. Suppose there are $n = 9$ patches arranged and connected as in Figure 1. We assume that $L_{ij} \in \{0, 1\}$ with $L_{ij} = 1$ whenever patches i and j are connected by an arrow. In addition, $\gamma_j = 1$ and $\bar{S}_j(0) + \bar{I}_j(0) = 100$ for $j \in \Omega$, so that $\mathcal{R}_0^{[j]} = \beta_j$ and $N = 900$. Four numerical examples (see Figure 2) illustrate the values of S_j^* for $j \in \Omega$. Low-risk patches ($\mathcal{R}_0^{[j]} < 1$) are gray, and high-risk patches ($\mathcal{R}_0^{[j]} > 1$) are white. For $\mathcal{R}_0 > 1$ ($d_I < d_I^*$), the value of S_j^* was approximated by \tilde{S}_j , which was calculated using the iterative method (3.11) with $d_S \leq 10^{-5}$, $d_I = 1$, and $\sum_{j \in \Omega} \tilde{I}_j < 0.005$.

For the limiting DFE in Figure 2(a), susceptibles can persist only on low-risk patches. In this case, condition (1.6) of Theorem 2(c) is satisfied:

$$1 = \frac{1}{d_I} > \max_{k \in H^+} \left\{ \frac{L_k^-}{\beta_k - \gamma_k} \right\} + \max_{k \in H^-} \left\{ \frac{L_k^+}{\beta_k - \gamma_k} \right\} = \frac{2}{0.5} - \frac{2}{0.5} = 0.$$

FIG. 1. *Nine patches connected at their boundaries.*

For the limiting DFE in Figure 2(b), susceptibles can persist on several high-risk patches. In this case, condition (1.7) of Theorem 2(d) is satisfied for $j = 2, 5, 6$,

$$1 = \frac{1}{d_I} < \frac{L_j^-}{\beta_j - \gamma_j} + \min_{k \in H^-} \left\{ \frac{L_k^+}{\beta_k - \gamma_k} \right\} = \frac{\{2 \text{ or } 1\}}{0.25} - \frac{1}{0.5} = \{6 \text{ or } 2\},$$

but not for $j = 3$:

$$1 = \frac{1}{d_I} > \frac{L_3^-}{\beta_3 - \gamma_3} + \min_{k \in H^-} \left\{ \frac{L_k^+}{\beta_k - \gamma_k} \right\} = \frac{0}{0.25} - \frac{1}{0.5} = -2.$$

We consider Figure 2(c), (d) in the Discussion.

2. The DFE. Throughout this section, we assume that (A1)–(A3) hold and that N is fixed.

2.1. Existence and uniqueness of the DFE. Equation (1.4) has a unique disease-free solution, and it is spatially homogeneous.

LEMMA 2.1. *A DFE $(\hat{S}, 0)$ exists, it is unique, and it is given by $\hat{S}_j = N/n$ for $j \in \Omega$.*

Proof. It is clear from (1.4) that $(\hat{S}, 0)$, with $\hat{S}_j = N/n$ for $j \in \Omega$, is a DFE. Now, let $(\tilde{S}, 0)$ be any DFE. Choose $m \in \Omega$ such that $\tilde{S}_m = \min\{\tilde{S}_j : j \in \Omega\}$. Setting $\tilde{I} = 0$ in (1.4a) with $j = m$ leads to $\sum_{k \in \Omega} L_{mk}(\tilde{S}_k - \tilde{S}_m) = 0$. The minimality of \tilde{S}_m implies that $\tilde{S}_k = \tilde{S}_m$ whenever $L_{mk} > 0$. Let $j \in \Omega$ with $j \neq m$. The irreducibility of L implies that there exists a chain from j to m , i.e., a sequence $j_1, j_2, \dots, j_s \in \Omega$ with $j_1 = j$ and $j_s = m$ such that $L_{j_p j_{p+1}} > 0$ for $1 \leq p \leq s-1$. Thus $\tilde{S}_{j_p} = \tilde{S}_{j_{p+1}}$ for $1 \leq p \leq s-1$. We conclude that $\tilde{S}_j = \tilde{S}_m$. Since j is arbitrary, we must have $\tilde{S}_j = \tilde{S}_m$ for all $j \in \Omega$. In view of (1.4c) with $\tilde{I} = 0$, we obtain $\tilde{S}_j = N/n$ for $j \in \Omega$. \square

225	0	225
0	0	0
225	0	225

(a)

126.4	57.4	0
141.1	90.2	57.4
159.9	141.1	126.4

(b)

147.8	0	0
172.6	42.4	0
216.8	172.6	147.8

(c)

123.75	101.25	123.75
101.25	0	101.25
123.75	101.25	123.75

(d)

FIG. 2. *The limiting DFE under four parameter conditions. (a) $\mathcal{R}_0 = 1.20$, $\mathcal{R}_0^{[5]} = 2$, $\mathcal{R}_0^{[j]} = 1.5$, and $\mathcal{R}_0^{[k]} = 0.5$ for $j = 2, 4, 6, 8$ and $k = 1, 3, 7, 9$; (b) $\mathcal{R}_0 = 1.51$, $\mathcal{R}_0^{[3]} = 3$, $\mathcal{R}_0^{[j]} = 1.25$, and $\mathcal{R}_0^{[k]} = 0.5$ for $j = 2, 5, 6$ and $k = 1, 4, 7, 8, 9$; (c) $\mathcal{R}_0 = 1.58$, $\mathcal{R}_0^{[3]} = 3$, $\mathcal{R}_0^{[j]} = 1.5$, and $\mathcal{R}_0^{[k]} = 0.5$ for $j = 2, 5, 6$ and $k = 1, 4, 7, 8, 9$; (d) $\mathcal{R}_0 = 1.03$, $\mathcal{R}_0^{[5]} = 3$, and $\mathcal{R}_0^{[j]} = 0.5$ for $j \neq 5$.*

2.2. Stability of the DFE. Applying Lemma 2.1, we can calculate the basic reproduction number \mathcal{R}_0 for (1.1) using the next generation approach (Diekmann, Heesterbeek, and Metz (1990), Diekmann and Heesterbeek (2000), van den Driessche and Watmough (2002)). Since there are n patches, the basic reproduction number will be the spectral radius of an $n \times n$ nonnegative matrix. It is known that if $\mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable, and if $\mathcal{R}_0 > 1$, then the DFE is unstable (van den Driessche and Watmough (2002)).

LEMMA 2.2. *The basic reproduction number for (1.1) is the spectral radius of the next generation matrix,*

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where $F = \text{diag}(\beta_j)$ and $V = \text{diag}(\gamma_j + d_I L_j) - d_I L$.

Proof. We can write (1.1b) as

$$\frac{d\bar{I}}{dt} = \mathcal{F} - \mathcal{V},$$

where \mathcal{F} is the vector of new infections and \mathcal{V} is the vector of transitions in the n infected states. Linearization of this system about the DFE yields

$$\frac{dx}{dt} = (F - V)x,$$

where F and V are the Jacobian matrices of \mathcal{F} and \mathcal{V} , respectively, evaluated at the DFE. The eigenvalues of $(F - V)$ have negative real part if and only if $\mathcal{R}_0 = \rho(FV^{-1}) < 1$ (van den Driessche and Watmough (2002)). \square

We now show that if $\mathcal{R}_0 < 1$, then the disease always becomes extinct; i.e., the DFE is globally asymptotically stable.

LEMMA 2.3. *If $\mathcal{R}_0 < 1$, then $(\bar{S}, \bar{I}) \rightarrow (\hat{S}, 0)$ as $t \rightarrow \infty$.*

Proof. Suppose that $\mathcal{R}_0 < 1$. We will use the comparison principle to show that $\bar{I}(t) \rightarrow 0$ as $t \rightarrow \infty$. To begin, observe from (1.1b) that

$$\frac{d\bar{I}_j}{dt} \leq d_I \sum_{k \in \Omega} L_{jk} \bar{I}_k + (\beta_j - \gamma_j - d_I L_j) \bar{I}_j, \quad j \in \Omega,$$

or equivalently

$$\frac{d\bar{I}}{dt} \leq (F - V)\bar{I},$$

where F and V are as in Lemma 2.2. The linear comparison system

$$\frac{dx}{dt} = (F - V)x, \quad x(0) = \bar{I}(0),$$

which is monotone, has eigenvalues with negative real part because $\mathcal{R}_0 < 1$ (van den Driessche and Watmough (2002)). Consequently, $x(t) \rightarrow 0$ as $t \rightarrow \infty$. By comparison, $\bar{I}(t) \rightarrow 0$ as $t \rightarrow \infty$. \square

The global asymptotic stability of the DFE when $\mathcal{R}_0 < 1$ implies that there can be no EE in this case. In section 3, we consider what happens when $\mathcal{R}_0 > 1$.

3. The endemic equilibrium. Throughout this section, we again assume that (A1)–(A3) hold and that N is fixed.

3.1. Equivalent problems. It will be useful to consider several alternative statements of the equilibrium problem. We present here the first such equivalent problem.

LEMMA 3.1. *The pair (\tilde{S}, \tilde{I}) is a solution of (1.4) if and only if (\tilde{S}, \tilde{I}) is a solution of*

$$(3.1a) \quad \kappa = d_S \tilde{S}_j + d_I \tilde{I}_j, \quad j \in \Omega,$$

$$(3.1b) \quad 0 = d_I \sum_{k \in \Omega} L_{jk} (\tilde{I}_k - \tilde{I}_j) + \tilde{I}_j \left(\beta_j - \gamma_j - \frac{\beta_j \tilde{I}_j}{\tilde{S}_j + \tilde{I}_j} \right), \quad j \in \Omega,$$

$$(3.1c) \quad N = \sum_{j \in \Omega} (\tilde{S}_j + \tilde{I}_j),$$

where κ is some positive constant that is independent of $j \in \Omega$.

Proof. Suppose first that (\tilde{S}, \tilde{I}) is a solution of (1.4). We will show that there exists some $\kappa > 0$ such that (\tilde{S}, \tilde{I}) satisfies (3.1a). Summing (1.4a) and (1.4b) produces the relation

$$d_S \sum_{k \in \Omega} L_{jk}(\tilde{S}_k - \tilde{S}_j) + d_I \sum_{k \in \Omega} L_{jk}(\tilde{I}_k - \tilde{I}_j) = 0, \quad j \in \Omega.$$

We rearrange to get

$$\sum_{k \in \Omega} (L_{jk}/L_j) (d_S \tilde{S}_k + d_I \tilde{I}_k) = d_S \tilde{S}_j + d_I \tilde{I}_j, \quad j \in \Omega.$$

We can express this system of equations in matrix-vector form as

$$A (d_S \tilde{S} + d_I \tilde{I}) = d_S \tilde{S} + d_I \tilde{I},$$

where $A = (L_{jk}/L_j)$. Clearly, $A \geq 0$ because $L \geq 0$ and $L_j > 0$ for $j \in \Omega$. Moreover, since A and L are associated with the same adjacency matrix, it follows that A is irreducible. According to the Frobenius theorem (Gantmacher (1960), Theorem 2, p. 53), A has a largest (or *principal*) eigenvalue μ which is real, and μ has a one-dimensional eigenspace $\langle \psi \rangle$ for some positive eigenvector ψ . No other eigenvalue of A has a positive corresponding eigenvector. Since A is a stochastic matrix, the positive vector $x = (1, 1, \dots, 1)^t$ is an eigenvector for A belonging to the eigenvalue 1. It follows from the remarks above that $\mu = 1$ and we may take $\psi = x$. As the vector $d_S \tilde{S} + d_I \tilde{I}$ is also an eigenvector for A belonging to the eigenvalue 1, we conclude that $d_S \tilde{S} + d_I \tilde{I} = \kappa \psi$ for some $\kappa \in \mathbb{R}$. Since $d_S \tilde{S}_j + d_I \tilde{I}_j > 0$ for at least one $j \in \Omega$ (because $N > 0$) it must be that $\kappa > 0$. Therefore (\tilde{S}, \tilde{I}) satisfies (3.1a) for some $\kappa > 0$. The fact that (\tilde{S}, \tilde{I}) satisfies (3.1b) and (3.1c) is clear by inspection. If (\tilde{S}, \tilde{I}) is a solution of (3.1) for some $\kappa > 0$, then it follows from a direct calculation that (\tilde{S}, \tilde{I}) satisfies (1.4). \square

For our second equivalent formulation of the equilibrium problem, let

$$(3.2) \quad S_j = \frac{\tilde{S}_j}{\kappa} \quad \text{and} \quad I_j = \frac{d_I \tilde{I}_j}{\kappa},$$

where κ is as in Lemma 3.1. Let $S = (S_j)$, $I = (I_j)$, and

$$(3.3) \quad f_j(u) = \beta_j \left(1 - \frac{d_S u}{d_I + (d_S - d_I)u} \right) - \gamma_j, \quad u \in [0, 1] \quad \text{and} \quad j \in \Omega.$$

Observe that if $\beta_j > 0$, then f_j decreases from $\beta_j - \gamma_j$ to $-\gamma_j$ as u increases from 0 to 1. The next result follows from a direct calculation.

LEMMA 3.2. *The pair (\tilde{S}, \tilde{I}) is a solution of (3.1) if and only if (S, I) is a solution of*

$$(3.4a) \quad 1 = d_S S_j + I_j, \quad j \in \Omega,$$

$$(3.4b) \quad 0 = d_I \sum_{k \in \Omega} L_{jk} (I_k - I_j) + I_j f_j(I_j), \quad j \in \Omega,$$

$$(3.4c) \quad \kappa = \frac{d_I N}{\sum_{j \in \Omega} (d_I S_j + I_j)}.$$

The benefit of this second formulation is that (3.4b) depends on I but not S . Thus, once I is determined, it is then a simple matter to determine S from (3.4a) and κ from (3.4c). Observe that κ is in a one-to-one correspondence with N .

3.2. An eigenvalue problem. The linear eigenvalue problem associated with (3.1b) at the DFE is

$$(3.5) \quad d_I \sum_{k \in \Omega} L_{jk}(\psi_k - \psi_j) + (\beta_j - \gamma_j)\psi_j + \lambda\psi_j = 0, \quad j \in \Omega.$$

Observe that (3.5) can be written as

$$d_I \sum_{k \in \Omega} L_{jk}\psi_k + (\beta_j + \theta - \gamma_j - d_I L_j)\psi_j = (\theta - \lambda)\psi_j, \quad j \in \Omega,$$

where $\theta = \max\{\gamma_j + d_I L_j : j \in \Omega\}$, and this equation can be written in the equivalent matrix-vector form $(d_I L + D)\psi = (\theta - \lambda)\psi$, where $D = \text{diag}(\beta_j + \theta - \gamma_j - d_I L_j)$ and $\psi = (\psi_j)$. Thus, (λ, ψ) is a solution of (3.5) if and only if $(\mu, \psi) = (\theta - \lambda, \psi)$ is a solution of

$$(3.6) \quad Q\psi = \mu\psi,$$

where $Q = d_I L + D$.

LEMMA 3.3. *The matrix Q has all real eigenvalues, and it has a largest eigenvalue $\mu^* = \mu^*(d_I)$, which is positive. This eigenvalue μ^* has a one-dimensional eigenspace $\langle \phi \rangle$, where $\phi > 0$. Furthermore, no other eigenvalue of Q has a positive corresponding eigenvector.*

Proof. By construction, $Q_{jk} = d_I L_{jk} \geq 0$ for $j, k \in \Omega$ with $j \neq k$, and $Q_{jj} \geq d_I L_{jj} + \beta_j \geq 0$ for $j \in \Omega$. Therefore, Q is nonnegative. Moreover, Q is irreducible because Q and L are associated with adjacency matrices whose off-diagonal entries are the same. The stated properties of Q now follow from the symmetry of L (which implies that the eigenvalues of Q are real) and the Frobenius theorem (Gantmacher (1960)). \square

LEMMA 3.4. *Define $\lambda^* = \lambda^*(d_I) = \theta - \mu^*(d_I)$ and let $\phi > 0$ be as in Lemma 3.3. Then*

- (a) λ^* is real and (λ^*, ϕ) satisfies (3.5), i.e.,

$$(3.7) \quad d_I \sum_{k \in \Omega} L_{jk}(\phi_k - \phi_j) + (\beta_j - \gamma_j)\phi_j + \lambda^*\phi_j = 0, \quad j \in \Omega.$$

Moreover, (λ^, ψ) satisfies (3.5) if and only if $\psi \in \langle \phi \rangle$. Finally, if (λ, ψ) satisfies (3.5) with $\lambda \neq \lambda^*$, then $\lambda > \lambda^*$ and $\psi_j \leq 0$ for some $j \in \Omega$.*

- (b) λ^* is a strictly monotone increasing function of $d_I > 0$.
(c) $\lambda^* \rightarrow \min\{\gamma_j - \beta_j : j \in \Omega\}$ as $d_I \rightarrow 0$.
(d) $\lambda^* \rightarrow \frac{\Sigma_\gamma - \Sigma_\beta}{n}$ as $d_I \rightarrow \infty$.
(e) If $\Sigma_\beta \geq \Sigma_\gamma$, then $\lambda^* < 0$ for all $d_I > 0$.
(f) If $\Sigma_\beta < \Sigma_\gamma$, then the equation $\lambda^*(d_I) = 0$ has a unique positive root denoted by d_I^* . Furthermore, if $d_I < d_I^*$, then $\lambda^* < 0$, and if $d_I > d_I^*$, then $\lambda^* > 0$.

The proof of Lemma 3.4 appears in Appendix B. In view of Lemma 3.4(e), (f), let us define $d_I^* = \infty$ when $\Sigma_\beta \geq \Sigma_\gamma$. We now connect λ^* to the basic reproduction number \mathcal{R}_0 .

LEMMA 3.5. *Let \mathcal{R}_0 and λ^* be as in Lemmas 2.2 and 3.4, respectively. Then*

- (a) $\mathcal{R}_0 < 1$ if and only if $\lambda^* > 0$;
(b) $\mathcal{R}_0 > 1$ if and only if $\lambda^* < 0$.

Proof. Observe from (3.7) that

$$(3.8) \quad (F - V)\phi + \lambda^*\phi = 0,$$

where F and V are defined as in Lemma 2.2. Also, since $F - V$ is symmetric, its eigenvalues are all real. Finally, recall from van den Driessche and Watmough (2002) that (i) $\mathcal{R}_0 < 1$ if and only if $F - V$ has all negative eigenvalues, and (ii) $\mathcal{R}_0 > 1$ if and only if $F - V$ has a positive eigenvalue.

- (a) Suppose first that $\mathcal{R}_0 < 1$. We see from (3.8) that $(-\lambda^*)$ is an eigenvalue of $F - V$. Since $F - V$ has all negative eigenvalues, we obtain $\lambda^* > 0$. Now suppose that $\lambda^* > 0$. Equation (3.8) and Lemma 3.4(a) imply that $(-\lambda^*)$ is the largest eigenvalue of $F - V$. Thus, all the eigenvalues of $F - V$ are negative, and consequently $\mathcal{R}_0 < 1$.
- (b) Suppose first that $\mathcal{R}_0 > 1$. Then $F - V$ has a positive eigenvalue μ . Equation (3.8) and Lemma 3.4(a) imply that $\lambda^* \leq -\mu < 0$, i.e., $\lambda^* < 0$. Now suppose that $\lambda^* < 0$. We see from (3.8) that $\mu = -\lambda^*$ is a positive eigenvalue of $F - V$, and hence that $\mathcal{R}_0 > 1$. \square

In the next section, we use λ^* and ϕ , rather than \mathcal{R}_0 , to obtain the existence of an EE when the DFE is unstable.

3.3. Existence of an EE.

LEMMA 3.6. *Suppose that $\mathcal{R}_0 > 1$. Then (3.4) has a nonnegative solution (S, I) , which can be chosen to satisfy $I \not\equiv 0$. Furthermore, this solution with $I \not\equiv 0$ is unique, $S > 0$, and $0 < I_j < 1$ for every $j \in \Omega$.*

Here we prove the existence of such an (S, I) , and in the next section we will demonstrate that it is unique. Suppose that $\mathcal{R}_0 > 1$. In view of (3.4b), consider the related system of differential equations

$$(3.9) \quad \frac{dI_j}{dt} = G_j(I) \stackrel{\text{def}}{=} d_I \sum_{k \in \Omega} L_{jk}(I_k - I_j) + I_j f_j(I_j), \quad j \in \Omega.$$

First, I is a solution of (3.4b) if and only if $G(I) = 0$, where $G = (G_j)$. Second, (3.9) defines a monotone dynamical system because L_{jk} is nonnegative when $j \neq k$. It follows that if \underline{I} and \bar{I} are ordered (i.e., $\underline{I} \leq \bar{I}$), and they are sub- and supersolutions of (3.9), respectively, i.e., $G(\underline{I}) \geq 0 \geq G(\bar{I})$, then there must exist some $I \in [\underline{I}, \bar{I}]$ such that $G(I) = 0$, where $[\underline{I}, \bar{I}] = \{I \in \mathbb{R}^n : \underline{I} \leq I \leq \bar{I}\}$ (Smith (1995)).

With $\phi > 0$ defined as in Lemma 3.3, we now show that $\underline{I} = \epsilon\phi$ and $\bar{I} = (1, 1, \dots, 1)^t$ can be chosen as sub- and supersolutions for (3.9) if ϵ is chosen to be positive and sufficiently small. We may assume that ϕ is chosen so that $\sum_{j \in \Omega} \phi_j^2 = 1$. Lemma 3.5(b) implies that $\lambda^* < 0$. In view of (3.3), define

$$g(u) = \frac{d_S u}{d_I + (d_S - d_I)u}, \quad u \in [0, 1].$$

We remark that g increases from 0 to 1 as u increases from 0 to 1. Observe from (3.3) and (3.7) that

$$\begin{aligned} G_j(\underline{I}) &= d_I \sum_{k \in \Omega} L_{jk}(\epsilon\phi_k - \epsilon\phi_j) + \epsilon\phi_j f_j(\epsilon\phi_j) \\ &= \epsilon \left[d_I \sum_{k \in \Omega} L_{jk}(\phi_k - \phi_j) + (\beta_j - \gamma_j)\phi_j - \beta_j\phi_j g(\epsilon\phi_j) \right] \\ &= \epsilon\phi_j [-\lambda^* - \beta_j g(\epsilon\phi_j)] \end{aligned}$$

is positive for $j \in \Omega$ when $0 < \epsilon \ll 1$. Therefore, \underline{I} is a subsolution of (3.9) for ϵ positive and sufficiently small. Next, since $G_j(\bar{I}) = f_j(1) = -\gamma_j$ is nonpositive for $j \in \Omega$, it follows that \bar{I} is a supersolution of (3.9). Also, it is obvious that $\underline{I} \leq \bar{I}$ if ϵ is chosen sufficiently small. We conclude from the remarks above that there must be an $I \in [\underline{I}, \bar{I}]$ with $G(I) = 0$. That is, there exists some I satisfying (3.4b) with $0 < I_j \leq 1$ for $j \in \Omega$. We argue by contradiction to show that I_j cannot be equal to 1 for any $j \in \Omega$. If $I_j = 1$ for all $j \in \Omega$, then $G_j(I) = -\gamma_j < 0$ for $j \in H^-$, a contradiction. If $I_j = 1$ and $I_m < 1$ for some $j, m \in \Omega$, then there exists a chain from j to m , i.e., a sequence $j_1, j_2, \dots, j_s \in \Omega$ with $j_1 = j$ and $j_s = m$ such that $L_{j_p j_{p+1}} > 0$ for $1 \leq p \leq s-1$. Thus, there exists some $k \in \Omega$ for which $I_{j_k} = 1$, $I_{j_{k+1}} < 1$, and $L_{j_k j_{k+1}} > 0$. But then $G_{j_k}(I) \leq d_I L_{j_k j_{k+1}}(I_{j_{k+1}} - I_{j_k}) - \gamma_{j_k} < 0$, again a contradiction. We conclude that $0 < I_j < 1$ for $j \in \Omega$. In view of (3.4a), let us define S by $1 = d_S S + I$. Then $S > 0$. Consequently, (S, I) is a positive solution of (3.4) with $I_j < 1$ for $j \in \Omega$.

For sake of completeness, and also for the purpose of proving uniqueness in the next section, we now proceed to construct an iteration algorithm to find I . This algorithm is also used to generate the numerical plots appearing in Figure 2. Equation (3.4b) can be written equivalently as

$$(3.10) \quad -d_I \sum_{k \in \Omega} L_{jk}(I_k - I_j) = F_j(I_j), \quad j \in \Omega,$$

where $F_j(u) = u f_j(u)$. Let $j \in \Omega$. By inspection, the function f_j in (3.3) and its derivative f_j' are bounded for $u \in [0, 1]$. We conclude that there exists some $M > 0$ (which can be chosen to be independent of j) such that $|F_j'(u)| < M$ for $u \in [0, 1]$. It follows that $F_j'(u) + M > 0$ for $u \in [0, 1]$. That is, $F_j(u) + Mu$ is a monotone increasing function of $u \in [0, 1]$. Since $F_j'(u) = f_j(u) + u f_j'(u) \leq f_j(u)$ for $u \in [0, 1]$, it follows that $f_j(u) + M > 0$ for $u \in [0, 1]$.

We now add MI_j to both sides of (3.10) to get

$$-d_I \sum_{k \in \Omega} L_{jk}(I_k - I_j) + MI_j = F_j(I_j) + MI_j, \quad j \in \Omega.$$

This equation inspires the vector iteration

$$(3.11) \quad -d_I \sum_{k \in \Omega} L_{jk}(I_k^{(l+1)} - I_j^{(l+1)}) + MI_j^{(l+1)} = F_j(I_j^{(l)}) + MI_j^{(l)}, \quad j \in \Omega,$$

with the index $l \geq 0$. This implicit scheme can be made explicit because the left-hand operator, which takes the form $A + M\mathcal{I}_n = M[(1/M)A + \mathcal{I}_n]$, is invertible for M sufficiently large. Let $I^{(l)} = (I_j^{(l)})$. For our purposes, we will set $I^{(0)} = \underline{I} = \epsilon\phi$ with ϵ taken to be sufficiently small so that \underline{I} is a subsolution of (3.9) satisfying $\underline{I} < \bar{I} = (1, 1, \dots, 1)^t$. Similarly, we define the iteration

$$(3.12) \quad -d_I \sum_{k \in \Omega} L_{jk}(I_k^{[l+1]} - I_j^{[l+1]}) + MI_j^{[l+1]} = F_j(I_j^{[l]}) + MI_j^{[l]}, \quad j \in \Omega,$$

for $l \geq 0$ with $I^{[0]} = \bar{I}$, a supersolution of (3.9). We want to show that

$$\underline{I} = I^{(0)} \leq I^{(1)} \leq \dots \leq I^{(n)} \leq \dots \leq I^{[n]} \leq \dots \leq I^{[1]} \leq I^{[0]} = \bar{I},$$

where the symbols surrounding the iteration index indicate the initial condition for the sequence. For convenience, we will refer to the sequences $I^{(l)}$ and $I^{[l]}$ as the *lower* and *upper sequences*, respectively.

It can be shown that all components of both sequences remain within the interval $[0, 1]$, that the lower sequence is nondecreasing, that the upper sequence is nonincreasing, and that an iterate of the lower sequence is always less than or equal to the corresponding iterate of the upper sequence. Let $\Delta I^{(l)} = I^{(l+1)} - I^{(l)}$, $\Delta I^{[l]} = I^{[l+1]} - I^{[l]}$, and $\Delta I^{\{l\}} = I^{\{l\}} - I^{(l)}$.

LEMMA 3.7. *The following statements hold:*

- (a) $I_j^{(l)}, I_j^{[l]} \in [0, 1]$ for $l \geq 0$ and $j \in \Omega$;
- (b) $\Delta I^{(l)} \geq 0$, $\Delta I^{[l]} \leq 0$, and $\Delta I^{\{l\}} \geq 0$ for $l \geq 0$.

The proof of this result appears in Appendix C. According to Lemma 3.7, the lower and upper sequences are both monotone and bounded. They also satisfy $\underline{I} \leq I^{(l)} \leq I^{[l]} \leq \bar{I}$ for $l \geq 0$. Therefore, there exist I^{\min} and I^{\max} such that $I^{(l)} \rightarrow I^{\min}$ and $I^{[l]} \rightarrow I^{\max}$ as $l \rightarrow \infty$. Clearly, $\underline{I} \leq I^{\min} \leq I^{\max} \leq \bar{I}$. Furthermore, since I^{\min} is a fixed point for (3.11), and I^{\max} is a fixed point for (3.12), each is a solution to (3.4b) with the property that $0 < I_j^{\min} \leq I_j^{\max} \leq 1$ for $j \in \Omega$. By an argument similar to the one given above, we obtain the stronger result that $0 < I_j^{\min} \leq I_j^{\max} < 1$ for $j \in \Omega$. In the next section, we show that $I_j^{\min} = I_j^{\max}$.

3.4. Uniqueness of the EE. Because we are interested only in those (S, I) that satisfy (3.4) with $S \geq 0$ and $I \geq 0$, we will assume throughout this section that if I is a solution to (3.4b), then $0 \leq I_j \leq 1$ for $j \in \Omega$.

LEMMA 3.8. *If I is a solution to (3.4b), then either $I \equiv 0$ or $I > 0$.*

Proof. We argue by contradiction. Suppose that I is a solution of (3.4b) with $I \not\equiv 0$ and $I \not> 0$. Then there exist nonempty subsets K^- and K^+ of Ω with $I_j = 0$ for $j \in K^-$, $I_j > 0$ for $j \in K^+$, and $K^- \cup K^+ = \Omega$. Equation (3.4b) implies that $\sum_{k \in \Omega} L_{jk} I_k = 0$ for $j \in K^-$. The nonnegativity of L and I implies that $L_{jk} I_k = 0$ for $j \in K^-$ and $k \in \Omega$. Since $I_k > 0$ when $k \in K^+$, we must have $L_{jk} = 0$ when $j \in K^-$ and $k \in K^+$. But this contradicts the irreducibility of L . We conclude that either $I \equiv 0$ or $I > 0$. \square

The following lemma justifies our referring to I^{\min} and I^{\max} as *minimal* and *maximal* solutions, respectively.

LEMMA 3.9. *If I is a positive solution to (3.4b), then $I \in [I^{\min}, I^{\max}]$.*

Proof. Choose ϵ small enough so that $\underline{I} = I^{(0)} \leq I \leq I^{[0]} = \bar{I}$. Arguments similar to the one used in the proof of Lemma 3.7(b) show that $I^{(l)} \leq I \leq I^{[l]}$ for $l \geq 0$. The conclusion follows by letting $l \rightarrow \infty$. \square

We now show that if two positive solutions of (3.4b) are ordered, then they are either strictly ordered or they are equal.

LEMMA 3.10. *If I^- and I^+ are positive solutions to (3.4b) with $I^- \leq I^+$, then either $I^- < I^+$ or $I^- \equiv I^+$.*

Proof. We argue by contradiction. Suppose that $I^- = (I_j^-)$ and $I^+ = (I_j^+)$ are positive solutions to (3.4b) with $I^- \leq I^+$, and that neither $I^- < I^+$ nor $I^- \equiv I^+$. Then there exist nonempty and disjoint subsets K^- and K^+ of Ω , whose union forms all of Ω , and with the property that $I_j^- < I_j^+$ for $j \in K^-$ and $I_j^- = I_j^+$ for $j \in K^+$. We subtract (3.4b) with $I = I^-$ from (3.4b) with $I = I^+$, and use the fact that $I_j^- = I_j^+$ for $j \in K^+$, to get $\sum_{k \in K^-} L_{jk} (I_k^+ - I_k^-) = 0$ for $j \in K^+$. We sum only over $k \in K^-$ because $I_k^+ = I_k^-$ for $k \in K^+$. By definition, the expression $I_k^+ - I_k^-$ is positive for $k \in K^-$. Consequently, $L_{jk} = 0$ for $j \in K^+$ and $k \in K^-$. But this contradicts the irreducibility of L . We conclude that either $I^- < I^+$ or $I^- \equiv I^+$. \square

LEMMA 3.11. *If I^* and I^{**} are positive solutions to (3.4b), then $I^* \equiv I^{**}$.*

Proof. We argue by contradiction. Suppose that I^* and I^{**} are positive solutions to (3.4b) with $I^* \not\equiv I^{**}$. Then $I^*, I^{**} \in [I^{\min}, I^{\max}]$, by Lemma 3.9. Since $I^* \not\equiv I^{**}$, it follows that $I^{\min} \not\equiv I^{\max}$. We conclude from the relation $I^{\min} \leq I^{\max}$ and Lemma 3.10 that $I^{\min} < I^{\max}$. So, without loss of generality, we may assume that $I^* < I^{**}$, for otherwise we may replace I^* with I^{\min} and I^{**} with I^{\max} . We substitute $I^* = (I_j^*)$ and $I^{**} = (I_j^{**})$ individually into (3.4b) to get

$$\begin{aligned} d_I \sum_{k \in \Omega} L_{jk}(I_k^* - I_j^*) + I_j^* f_j(I_j^*) &= 0, \quad j \in \Omega, \\ d_I \sum_{k \in \Omega} L_{jk}(I_k^{**} - I_j^{**}) + I_j^{**} f_j(I_j^{**}) &= 0, \quad j \in \Omega. \end{aligned}$$

We multiply both sides of the first equation by I_j^{**} and both sides of the second equation by I_j^* , subtract the resulting equations, and then sum over all $j \in \Omega$ to get

$$d_I \sum_{j, k \in \Omega} L_{jk} \left[I_j^{**} I_k^* - I_j^* I_k^{**} \right] + \sum_{j \in \Omega} I_j^* I_j^{**} \left[f_j(I_j^*) - f_j(I_j^{**}) \right] = 0.$$

The symmetry of L implies that the first sum vanishes, and the second sum is non-negative because $I_j^* I_j^{**} > 0$ and $f_j(I_j^*) \geq f_j(I_j^{**})$ for $j \in \Omega$. The fact that $\beta_k > 0$ for $k \in H^+$ implies that $f_k(I_k^*) > f_k(I_k^{**})$, and thus the second sum is in fact positive, a contradiction. We conclude that $I^* \equiv I^{**}$. \square

Lemmas 3.9 and 3.11 imply that (3.4b) has a unique positive solution given by $I \stackrel{\text{def}}{=} I^{\min} = I^{\max}$. We conclude from Lemma 3.8 that I is the only nonnegative solution of (3.4b) satisfying $I \not\equiv 0$. We have completed the proof of Lemma 3.6. The next result follows from Lemmas 3.2 and 3.6 and (3.2).

LEMMA 3.12. *Suppose that $\mathcal{R}_0 > 1$. Then (1.4) has a nonnegative solution (\tilde{S}, \tilde{I}) which satisfies $\tilde{I} \not\equiv 0$. Furthermore, this solution is unique; it is given by $(\tilde{S}, \tilde{I}) = (\kappa S, \kappa I / d_I)$, where κ is as in (3.4c); and $\tilde{I} > 0$.*

We have shown that a unique EE exists when $\mathcal{R}_0 > 1$ and that it satisfies $\tilde{I} > 0$. In the next section, we consider the asymptotic behavior of the EE as $d_S \rightarrow 0$.

4. Asymptotic behavior of the endemic equilibrium. Throughout this section, we still assume that (A1)–(A3) hold and that N is fixed. We also assume that $\mathcal{R}_0 > 1$, so that Lemma 3.6 for (S, I) and Lemma 3.12 for (\tilde{S}, \tilde{I}) always apply.

4.1. The limiting DFE. Observe that \tilde{S} , \tilde{I} , and κ are all functions of d_S in (1.4) and (3.1). First, we determine the asymptotic behavior of \tilde{I} and κ .

LEMMA 4.1. *As $d_S \rightarrow 0$, $\kappa \rightarrow 0$ and $\tilde{I} \rightarrow 0$.*

Proof. We first show that $\kappa \rightarrow 0$ as $d_S \rightarrow 0$. Let $j \in H^-$ and \hat{I}_j be a limit point of \tilde{I}_j as $d_S \rightarrow 0$. Equation (1.4a) and the nonnegativity of β_j , \tilde{S}_j , and \tilde{I}_j imply that

$$d_S \sum_{k \in \Omega} L_{jk} (\tilde{S}_k - \tilde{S}_j) \leq \tilde{I}_j (\beta_j - \gamma_j).$$

Since $\tilde{S}_k \in [0, N]$ for $k \in \Omega$, it follows that the left-hand side vanishes as $d_S \rightarrow 0$. Since $\beta_j < \gamma_j$, it must be that $\hat{I}_j \leq 0$. But $\hat{I}_j \geq 0$ because $\tilde{I}_j > 0$ for $d_S > 0$. We conclude that $\hat{I}_j = 0$. Thus, $\tilde{I}_j \rightarrow 0$ as $d_S \rightarrow 0$ for all $j \in H^-$. Let $k \in H^-$ be fixed. Equation (3.1a) implies that $\kappa = d_S \tilde{S}_k + d_I \tilde{I}_k$. The product $d_S \tilde{S}_k \rightarrow 0$ as $d_S \rightarrow 0$ because $\tilde{S}_k \in [0, N]$, and $d_I \tilde{I}_k \rightarrow 0$ as $d_S \rightarrow 0$ by the argument above. Therefore, $\kappa \rightarrow 0$ as $d_S \rightarrow 0$.

We now show that $\tilde{I} \rightarrow 0$. Let $j \in \Omega$. Again, (3.1a) specifies that $\kappa = d_S \tilde{S}_j + d_I \tilde{I}_j$. The left-hand side vanishes as $d_S \rightarrow 0$ by part (a). The product $d_S \tilde{S}_j \rightarrow 0$ as $d_S \rightarrow 0$ because $\tilde{S}_j \in [0, N]$. We conclude that $\tilde{I}_j \rightarrow 0$ as $d_S \rightarrow 0$. \square

So that we may determine the asymptotic behavior of \tilde{S} , we first consider I in (3.2) as a function of d_S .

LEMMA 4.2. *I_j is a monotone decreasing function of d_S for each $j \in \Omega$.*

Proof. Suppose that $0 < d_{S_1} < d_{S_2}$, and let I^1 and I^2 be corresponding solutions to (3.4b) with $0 < I_j^1, I_j^2 < 1$ for $j \in \Omega$. Then

$$(4.1a) \quad d_I \sum_{k \in \Omega} L_{jk}(I_k^1 - I_j^1) + I_j^1 f_j(I_j^1, d_{S_1}) = 0, \quad j \in \Omega,$$

$$(4.1b) \quad d_I \sum_{k \in \Omega} L_{jk}(I_k^2 - I_j^2) + I_j^2 f_j(I_j^2, d_{S_2}) = 0, \quad j \in \Omega,$$

where

$$f_j(u, d_S) = \beta_j \left(1 - \frac{d_S u}{d_S u + d_I(1-u)} \right) - \gamma_j, \quad u \in [0, 1] \text{ and } j \in \Omega.$$

It is easy to see that $\partial f_j / \partial d_S \leq 0$. It follows from this fact and (4.1b), with d_{S_1} in place of d_{S_2} , that

$$d_I \sum_{k \in \Omega} L_{jk}(I_k^2 - I_j^2) + I_j^2 f_j(I_j^2, d_{S_1}) \geq 0, \quad j \in \Omega.$$

Thus, I^2 is a subsolution of (4.1a). Again, $\bar{I} = (1, 1, \dots, 1)^t$ is a supersolution of (4.1a). Also, $I^2 < \bar{I}$. By the iteration method presented in sections 3.3 and 3.4, (4.1a) has a unique solution $I^1 \in [I^2, \bar{I}]$. We conclude that $I^1 \geq I^2$. \square

Recall that $0 < I_j < 1$ for each $j \in \Omega$. The above lemma implies that for every $j \in \Omega$ there exists some I_j^* such that as $d_S \rightarrow 0$,

$$(4.2) \quad I_j \rightarrow I_j^* \quad \text{and} \quad 0 < I_j^* \leq 1.$$

Let $I^* = (I_j^*)$. It remains to establish conditions under which $0 < I_j^* < 1$ or $I_j^* = 1$. Let

$$J^- = \{j \in \Omega : 0 < I_j^* < 1\} \quad \text{and} \quad J^+ = \{j \in \Omega : I_j^* = 1\}.$$

Observe that $J^- \cup J^+ = \Omega$. We will need to know that J^- is nonempty.

LEMMA 4.3. $H^- \subseteq J^-$.

Proof. We argue by contradiction. Suppose that there exists some $j \in H^-$ with $j \in J^+$. Then $\beta_j < \gamma_j$ and $I_j^* = 1$. In view of (3.2), we multiply both sides of (3.1b) by d_I/κ and drop the nonnegative term $\beta_j \tilde{I}_j / (\tilde{S}_j + \tilde{I}_j)$ to get

$$d_I \sum_{k \in \Omega} L_{jk}(I_k - I_j) + I_j(\beta_j - \gamma_j) \geq 0.$$

Letting $d_S \rightarrow 0$ on both sides yields

$$d_I \sum_{k \in \Omega} L_{jk}(I_k^* - 1) + \beta_j - \gamma_j \geq 0.$$

The negativity of $\beta_j - \gamma_j$ implies that

$$\sum_{k \in \Omega} L_{jk}(I_k^* - 1) > 0.$$

But this inequality contradicts (4.2). We conclude that if $j \in H^-$, then $j \in J^-$. \square

We are now in a position to determine the asymptotic behavior of \tilde{S}_j .

LEMMA 4.4. *The following statements hold:*

- (a) $\kappa/d_S \rightarrow N^* \stackrel{\text{def}}{=} N / \sum_{j \in \Omega} (1 - I_j^*)$ as $d_S \rightarrow 0$;
- (b) $\tilde{S} \rightarrow S^*$ as $d_S \rightarrow 0$, where $S_j^* \stackrel{\text{def}}{=} (1 - I_j^*)N^*$;
- (c) $S^* \geq 0$ and $\sum_{j \in \Omega} S_j^* = N$.

Proof.

- (a) Equations (3.1a), (3.1c), and (3.2) imply that

$$N = \sum_{j \in \Omega} \left(\frac{\kappa - d_I \tilde{I}_j}{d_S} \right) + \sum_{j \in \Omega} \tilde{I}_j = \frac{\kappa}{d_S} \sum_{j \in \Omega} (1 - I_j) + \sum_{j \in \Omega} \tilde{I}_j.$$

Lemma 4.1 and (4.2) imply that

$$\frac{\kappa}{d_S} \rightarrow \frac{N}{\sum_{j \in \Omega} (1 - I_j^*)} \quad \text{as } d_S \rightarrow 0.$$

This limit is well defined because J^- is nonempty.

- (b) Again, (3.1a) and (3.2) imply that

$$\tilde{S}_j = \frac{\kappa - d_I \tilde{I}_j}{d_S} = (1 - I_j) \frac{\kappa}{d_S}.$$

Equation (4.2) and part (a) imply that $\tilde{S}_j \rightarrow (1 - I_j^*)N^*$ as $d_S \rightarrow 0$.

- (c) This part follows immediately from parts (a) and (b), the positivity of N , and (4.2). \square

4.2. The limiting DFE on high-risk patches. Observe from Lemma 4.4(b) that $S^* > 0$ on J^- and $S^* \equiv 0$ on J^+ . We know from Lemma 4.3 that J^- is nonempty because it contains H^- . Next we show that J^+ , which is a subset of H^+ , is also nonempty.

LEMMA 4.5. *J^+ is nonempty.*

Proof. We argue by contradiction. Suppose that J^+ is empty, i.e., $J^- = \Omega$. Multiply both sides of (3.1b) by d_I/κ to get

$$(4.3) \quad d_I \sum_{k \in \Omega} L_{jk}(I_k - I_j) + I_j \left(\beta_j - \gamma_j - \frac{\beta_j \tilde{I}_j}{\tilde{S}_j + \tilde{I}_j} \right) = 0, \quad j \in \Omega.$$

Since $I_j^* \in (0, 1)$ for $j \in \Omega$, we have from (3.4a) and (4.2) that $S_j = (1 - I_j)/d_S \rightarrow \infty$ as $d_S \rightarrow 0$ for $j \in \Omega$. It follows from this fact and (3.2) that

$$\frac{\beta_j \tilde{I}_j}{\tilde{S}_j + \tilde{I}_j} = \frac{\beta_j I_j}{d_I S_j + I_j} \rightarrow 0$$

as $d_S \rightarrow 0$ for $j \in \Omega$. Letting $d_S \rightarrow 0$ in (4.3), we get

$$d_I \sum_{k \in \Omega} L_{jk}(I_k^* - I_j^*) + I_j^*(\beta_j - \gamma_j) = 0, \quad j \in \Omega.$$

Thus $(\lambda, \psi) = (0, I^*)$ satisfies (3.5). Since $I^* > 0$, we obtain from Lemma 3.4(a) that $\lambda^* = 0$. But this contradicts Lemma 3.5(a). We conclude that J^+ is nonempty. \square

Next, we determine a condition under which J^+ is as large as it can be.

LEMMA 4.6. *If condition (1.6) holds, then $J^+ = H^+$.*

Proof. Recall that $J^+ \subseteq H^+$. We argue by contradiction to show that if condition (1.6) holds, then $H^+ \subseteq J^+$. Suppose that condition (1.6) holds and that there exists some $j \in H^+$ with the property that $j \in J^-$. Without loss of generality, we may assume that $I_j^* = \min\{I_k^* : k \in H^+\}$. Choose $m \in H^-$ so that $I_m^* = \min\{I_k^* : k \in H^-\}$. Letting $d_S \rightarrow 0$ in (3.4b) implies that

$$d_I \sum_{k \in \Omega} L_{jk}(I_k^* - I_j^*) + I_j^*(\beta_j - \gamma_j) = 0.$$

Here we used the fact that $0 < I_j^* < 1$. Since $\Omega = H^- \cup H^+$, we obtain

$$d_I \sum_{k \in H^+} L_{jk}(I_k^* - I_j^*) + d_I \sum_{k \in H^-} L_{jk}I_k^* + I_j^*(\beta_j - \gamma_j - d_I L_j^-) = 0.$$

The minimality of I_j^* over H^+ and I_m^* over H^- implies that

$$(4.4) \quad (d_I L_j^-)I_m^* \leq I_j^*(\gamma_j - \beta_j + d_I L_j^-).$$

A similar argument shows that

$$(4.5) \quad (d_I L_m^+)I_j^* \leq I_m^*(\gamma_m - \beta_m + d_I L_m^+).$$

We multiply corresponding sides of (4.4) and (4.5) together and simplify to get

$$(\gamma_j - \beta_j)(\gamma_m - \beta_m) + (\gamma_j - \beta_j)d_I L_m^+ + (\gamma_m - \beta_m)d_I L_j^- \geq 0.$$

We divide both sides by $d_I(\gamma_j - \beta_j)(\gamma_m - \beta_m)$, which is negative, and rearrange to get

$$\frac{1}{d_I} \leq \frac{L_j^-}{\beta_j - \gamma_j} + \frac{L_m^+}{\beta_m - \gamma_m} \leq \max_{j \in H^+} \left[\frac{L_j^-}{\beta_j - \gamma_j} \right] + \max_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right].$$

This contradicts (1.6). We conclude that $H^+ \subseteq J^+$, and therefore that $H^+ = J^+$. \square

Finally, we determine a condition under which J^+ is a proper subset of H^+ .

LEMMA 4.7. *If condition (1.7) holds for some $j \in H^+$, then $j \in J^-$.*

Proof. We argue by contradiction. Suppose that condition (1.7) holds for some $p \in H^+$, and that $p \in J^+$. Choose $m \in H^-$ such that $I_m^* = \max\{I_k^* : k \in H^-\} < 1$. We let $d_S \rightarrow 0$ in (3.4b) with $j = m$ to get

$$0 = d_I \sum_{k \in \Omega} L_{mk}(I_k^* - I_m^*) + I_m^*(\beta_m - \gamma_m).$$

We rearrange to get

$$0 = d_I \sum_{k \in H^+} L_{mk}I_k^* + d_I \sum_{k \in H^-} L_{mk}I_k^* + I_m^*(\beta_m - \gamma_m - d_I L_m).$$

The upper bound of 1 on I_k^* and the maximality of I_m^* imply that

$$0 \leq d_I L_m^+ + I_m^* (\beta_m - \gamma_m + d_I L_m^- - d_I L_m).$$

The relation $L_m^+ + L_m^- = L_m$ implies that

$$I_m^* (\gamma_m - \beta_m + d_I L_m^+) \leq d_I L_m^+.$$

The positivity of $\gamma_m - \beta_m$ implies that

$$(4.6) \quad I_m^* \leq \frac{d_I L_m^+}{\gamma_m - \beta_m + d_I L_m^+}.$$

Letting $d_S \rightarrow 0$ in (3.4b), we get

$$0 \leq d_I \sum_{k \in \Omega} L_{jk} (I_k^* - I_j^*) + I_j^* (\beta_j - \gamma_j), \quad j \in \Omega.$$

Again, we rearrange to get

$$0 \leq d_I \sum_{k \in H^+} L_{jk} I_k^* + d_I \sum_{k \in H^-} L_{jk} I_k^* + I_j^* (\beta_j - \gamma_j - d_I L_j), \quad j \in \Omega.$$

In particular, if $j = p$, then

$$0 \leq d_I L_p^+ + d_I \sum_{k \in H^-} L_{pk} I_k^* + (\beta_p - \gamma_p - d_I L_p).$$

The relation $L_p^+ + L_p^- = L_p$ and the maximality of I_m^* imply that

$$0 \leq d_I (I_m^* - 1) L_p^- + \beta_p - \gamma_p.$$

Equation (4.6) implies that

$$0 \leq d_I \left(\frac{d_I L_m^+}{\gamma_m - \beta_m + d_I L_m^+} - 1 \right) L_p^- + \beta_p - \gamma_p.$$

We rearrange to get

$$\frac{\beta_p - \gamma_p}{d_I} \geq \left(\frac{\gamma_m - \beta_m}{\gamma_m - \beta_m + d_I L_m^+} \right) L_p^-.$$

The positivity of $\gamma_m - \beta_m$ and $\beta_p - \gamma_p$ implies that

$$\frac{1}{d_I} \geq \frac{L_p^-}{\beta_p - \gamma_p} + \frac{L_m^+}{\beta_m - \gamma_m} \geq \frac{L_p^-}{\beta_p - \gamma_p} + \min_{k \in H^-} \left[\frac{L_k^+}{\beta_k - \gamma_k} \right].$$

But this contradicts (1.7) with $j = p$. We conclude that if (1.7) holds for some $p \in H^+$, then $p \in J^-$. \square

5. Discussion. We first mention some limiting cases for which we can simplify the expression for the basic reproduction number \mathcal{R}_0 . We next state some open problems that relate to our work, and then finish with some concluding remarks.

5.1. Limiting cases. In the general case, we will not be able to obtain a simple expression for \mathcal{R}_0 . However, we can compute an explicit expression for \mathcal{R}_0 in special cases.

In two limiting cases for n patches, the expression for \mathcal{R}_0 can be simplified. The basic reproduction number tends to the maximum ratio of the transmission rate to the recovery rate as infected movement becomes arbitrarily small ($\mathcal{R}_0 \rightarrow \max\{\beta_j/\gamma_j : j \in \Omega\}$ as $d_I \rightarrow 0$), and it tends to the average transmission rate divided by the average recovery rate as infected movement becomes arbitrarily large ($\mathcal{R}_0 \rightarrow \Sigma_\beta/\Sigma_\gamma$ as $d_I \rightarrow \infty$). The latter limit can be verified for a given value of n by calculating the limit V_∞^{-1} of V^{-1} as $d_I \rightarrow \infty$ (McCormack (2006)). For example, if $n = 2$ patches, then $F = \begin{pmatrix} \beta_1 & 0 \\ 0 & \beta_2 \end{pmatrix}$ and $V_\infty^{-1} = \frac{1}{\gamma_1 + \gamma_2} \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}$, so that the limiting value of \mathcal{R}_0 is $\rho(FV_\infty^{-1}) = \frac{\beta_1 + \beta_2}{\gamma_1 + \gamma_2}$.

In the general case that $n = 2$, then \mathcal{R}_0 in Lemma 2.2 becomes

$$\mathcal{R}_0 = \frac{\beta_2\gamma_1 + \beta_1\gamma_2 + d_I\ell(\beta_1 + \beta_2) + \sqrt{[\beta_2\gamma_1 - \beta_1\gamma_2 + d_I\ell(\beta_2 - \beta_1)]^2 + (2d_I\ell)^2\beta_1\beta_2}}{2[\gamma_1\gamma_2 + d_I\ell(\gamma_1 + \gamma_2)]},$$

where $\ell = L_{12} = L_{21}$. In this case, the condition $\mathcal{R}_0 < 1$ is equivalent to the following conditions:

$$\begin{aligned} (\beta_1 - \gamma_1 - d_I\ell) + (\beta_2 - \gamma_2 - d_I\ell) &< 0, \\ (\beta_1 - \gamma_1 - d_I\ell)(\beta_2 - \gamma_2 - d_I\ell) - (d_I\ell)^2 &> 0. \end{aligned}$$

That is, the eigenvalues of $F - V$ are negative if and only if the conditions above are satisfied.

5.2. Open problems. Some open mathematical questions remain in connection with this research.

- We conjecture that the basic reproductive number \mathcal{R}_0 is a monotone decreasing function of d_I . The difficulty in showing this directly is that, although V^{-1} is a function of d_I , a general expression for V^{-1} is not simple. If this conjecture is true, then $\max\{\beta_j/\gamma_j : j \in \Omega\}$ and $\Sigma_\beta/\Sigma_\gamma$ are upper and lower bounds, respectively, on \mathcal{R}_0 .
- We did not prove stability of the EE in Theorem 1. We conjecture that the EE globally attracts all solutions of (1.1) satisfying (1.2), and numerical simulations suggest that this is indeed the case. The uniform persistence of $\bar{I} = (\bar{I}_j)$ in (1.1) when the DFE is unstable has recently been established by Dhirasakdanon, Thieme, and van der Driessche (2007).
- We do not yet fully understand the asymptotic behavior of the EE as $d_S \rightarrow 0$. For example, condition (1.6) is not necessary for S_j^* to be zero on a patch. In Figure 2(c) susceptibles can persist on only one of four high-risk patches. In this case, condition (1.7) is satisfied for $j = 5$,

$$1 = \frac{1}{d_I} < \frac{L_5^-}{\beta_5 - \gamma_5} + \min_{k \in H^-} \left\{ \frac{L_k^+}{\beta_k - \gamma_k} \right\} = \frac{2}{0.5} - \frac{1}{0.5} = 2,$$

but neither condition (1.6) nor (1.7) is satisfied for $j = 2, 3, 6$. Similarly, condition (1.7) is probably not necessary for S_j^* to be positive on a patch. It is easy to see that if some high-risk patch ($j \in H^+$) is not directly connected to any low-risk patches ($L_j^- = 0$), then condition (1.7) cannot be satisfied because $L_k^+ / (\beta_k - \gamma_k)$ is nonpositive for $k \in H^-$. However, this does not rule

out the possibility that $S_j^* > 0$. In general, an open problem is to determine the distribution of high-risk patches for which S^* is either positive or zero when neither condition (1.6) nor (1.7) is satisfied. In Figure 2(d), susceptibles cannot persist on the single high-risk patch, and neither condition (1.6) nor (1.7) is satisfied:

$$\max_{j \in H^+} \left\{ \frac{L_j^-}{\beta_j - \gamma_j} \right\} = \frac{L_5^-}{\beta_5 - \gamma_5} = \frac{4}{2} = 2,$$

$$\min_{j \in H^-} \left\{ \frac{L_j^+}{\beta_j - \gamma_j} \right\} = -\frac{1}{0.5} = -2, \quad \text{and} \quad \max_{j \in H^-} \left\{ \frac{L_j^+}{\beta_j - \gamma_j} \right\} = 0.$$

As always, there are biological realities that we did not take into account, but which ecologists have suggested are important determinants of community dynamics.

- We neglect *population dynamics* (births or deaths) within the patches. At a very crude level, we can either ignore these dynamics on the grounds that epidemic dynamics often occur on a faster time scale than host demography, or we can say heuristically that death of an infected individual and subsequent replacement by a susceptible (in the absence of vertical transmission) is equivalent to a recovery event. Of course, either of these claims is an approximation, and it remains to be seen whether the results would be sensitive to such details.
- *Death during movement* may occur, especially if patches are separated by hostile “matrix” habitat. Adding this phenomenon might simply mean that some component of mortality (corresponding to a loss of infective potential, as argued in the previous point) scaled with d_I .
- *Density-dependent movement*—typically increasing rates of movement at higher population density, by organisms seeking to avoid competition—is generally an important factor in determining the behavior of spatial population dynamics models (Amarasekare (2004)).

These factors suggest possible directions for future exploration.

5.3. Mathematical and biological conclusions. Some of the relationships and techniques applied here have been applied by others. The relationship between the high rate of movement for infectives ($d_I > d_I^*$) and the basic reproduction number ($\mathcal{R}_0 < 1$) was noted by Salmani and van den Driessche (2006) in a two-patch SIS epidemic model. In addition, global stability of the DFE using comparison or monotone techniques has been applied by others (Arino et al. 2005; Arino and van den Driessche (2006); Wang and Mulone (2003); Wang and Zhao (2004)).

Our new results relate spatial heterogeneity, habitat connectivity, and rates of movement to disease persistence and extinction. We showed for populations with low mobility of susceptibles ($d_S \approx 0$) and moderate mobility of infectives ($0 \ll d_I < d_I^*$) that disease prevalence is very low ($\tilde{I} \approx 0$) in a spatial environment that includes both low-risk and high-risk patches. These results may have implications for disease control. If the environment is low-risk, but infectives move a lot, the disease may die out; conversely, restricting movement of infectives among patches (e.g., by habitat fragmentation) may allow the disease to persist and/or reemerge. In contrast, if a high-risk spatial environment can be modified to include low-risk patches (i.e., low transmission rates or high recovery rates) and if the mobility of susceptible individuals can be restricted, then it may be possible to eliminate the disease. In epidemiology,

quarantine attempts to prevent infected individuals from moving into a patch with a susceptible population; a *cordon sanitaire* attempts to restrict the movement of infected individuals out of a restricted area. The control strategy suggested by these results most closely resembles the movement restrictions imposed on *all* individuals (susceptible as well as infective) during the 2001 foot-and-mouth disease virus epidemic in Britain.

In a broader sense, these results fall under the ecological rubric of *source-sink dynamics*—population dynamics in heterogeneous environments with both “good” and “bad” patches (in our terminology, high- or low-risk patches, depending on whether we mean “good for the host” or “good for the disease”). The initially counterintuitive result that movement of infectives leads to disease extinction in a high-risk environment, which seems at odds with the idea of preventing disease from spreading between high-risk core groups and the general population (Jacquez, Simon, and Koopman (1995)), or between patches in a metapopulation (Hess (1996)), makes sense when we consider that (unlike in the core-group example), high infection rates are a property of the environment rather than of the individual. Ecologists usually want to prevent the extinction of threatened species; in contrast, epidemiologists want to promote the extinction of disease. However, ecologists have explored a broad range of questions, including evolutionary dynamics (Gomulkiewicz, Holt, and Barfield (1999)) and community structure (Namba and Hashimoto (2004)), in the context of source-sink dynamics. In the long run, linking the mathematical analyses of theoretical epidemiological and ecological models in heterogeneous landscapes can lead to broader mathematical and biological insights.

Appendix A. The irreducibility of L implies that, given any $j, k \in \Omega$ with $j \neq k$, there exists a distinct sequence $j_1, j_2, \dots, j_s \in \Omega$, with $j_1 = j$ and $j_s = k$, such that $L_{j_p j_{p+1}} > 0$ for $1 \leq p \leq s - 1$ (Seneta (1973), Exercise 1.3). We call such a sequence a *chain* from j to k . Second, the irreducibility of L implies that there exists no nonempty proper subset K of Ω with the property that $L_{jk} = 0$ for $j \in K$ and $k \notin K$ (Bapat and Raghavan (1997), Lemma 1.1.1). Finally, with L is associated an adjacency matrix $B = (B_{jk})$ for which $B_{jk} = 1$ if $L_{jk} > 0$ and $B_{jk} = 0$ if $L_{jk} = 0$. If the corresponding adjacency matrix for another nonnegative matrix A has the same off-diagonal entries as B , then A is also irreducible (Ortega (1987)).

Appendix B.

Proof of Lemma 3.4.

- (a) As θ and μ^* are both real, so is λ^* . The fact that (μ^*, ϕ) is a solution of (3.6) implies that (λ^*, ϕ) is a solution of (3.5). Since (λ^*, ψ) satisfies (3.5) if and only if (μ^*, ψ) satisfies (3.6), and (μ^*, ψ) is a solution of (3.6) if and only if $\psi \in \langle \phi \rangle$, it follows that (λ^*, ψ) is a solution of (3.5) if and only if $\psi \in \langle \phi \rangle$. Suppose that (λ, ψ) satisfies (3.5) with $\lambda \neq \lambda^*$. Then (μ, ψ) satisfies (3.6) with $\mu = \theta - \lambda \neq \theta - \lambda^* = \mu^*$. Lemma 3.3 implies that $\mu < \mu^*$ and $\psi_j \leq 0$ for some $j \in \Omega$. We conclude that $\lambda = \theta - \mu > \theta - \mu^* = \lambda^*$.
- (b) Observe from (3.7) that both ϕ and λ^* are functions of d_I . Both ϕ and λ^* are, in fact, differentiable functions of d_I by the implicit function theorem. We differentiate both sides of (3.7) by d_I to obtain

$$\sum_{k \in \Omega} L_{jk}(\phi_k - \phi_j) + d_I \sum_{k \in \Omega} L_{jk}(\phi'_k - \phi'_j) + (\beta_j - \gamma_j + \lambda^*)\phi'_j + (\lambda^*)'\phi_j = 0,$$

$$j \in \Omega.$$

It suffices to show that $(\lambda^*)' > 0$. We multiply both sides of the equation above by ϕ_j and sum over all $j \in \Omega$ to get

$$\begin{aligned} & \sum_{j,k \in \Omega} L_{jk}(\phi_k - \phi_j)\phi_j + d_I \sum_{j,k \in \Omega} L_{jk}(\phi'_k - \phi'_j)\phi_j \\ & + \sum_{j \in \Omega} (\beta_j - \gamma_j + \lambda^*)\phi_j\phi'_j + (\lambda^*)' \sum_{j \in \Omega} \phi_j^2 = 0. \end{aligned}$$

Equation (3.7) and the symmetry of L imply that the second and third sums on the left-hand side cancel:

$$\begin{aligned} \sum_{j \in \Omega} (\beta_j - \gamma_j + \lambda^*)\phi_j\phi'_j &= d_I \sum_{j,k \in \Omega} L_{jk}(\phi_j - \phi_k)\phi'_j \\ &= d_I \sum_{j,k \in \Omega} L_{jk}(\phi'_j - \phi'_k)\phi_j. \end{aligned}$$

Therefore,

$$\sum_{j,k \in \Omega} L_{jk}(\phi_k - \phi_j)\phi_j + (\lambda^*)' \sum_{j \in \Omega} \phi_j^2 = 0.$$

The symmetry of L implies that

$$(B.1) \quad (\lambda^*)' \sum_{j \in \Omega} \phi_j^2 = \frac{1}{2} \sum_{j,k \in \Omega} L_{jk}(\phi_j - \phi_k)^2.$$

Clearly, the right-hand side is nonnegative. We now show that it is in fact positive. We argue by contradiction. Suppose that

$$(B.2) \quad \sum_{j,k \in \Omega} L_{jk}(\phi_j - \phi_k)^2 = 0.$$

If $\phi_j = \phi_1$ for all $j \in \Omega$, then (3.7) and the positivity of ϕ imply that $\beta_j - \gamma_j + \lambda^* = 0$ for all $j \in \Omega$. But this is impossible, because H^- and H^+ are both nonempty. Therefore, it must be that $\phi_m \neq \phi_1$ for some $m \in \Omega$. The irreducibility of L implies that there exists a chain from 1 to m , i.e., a sequence $j_1, j_2, \dots, j_s \in \Omega$ with $j_1 = 1$ and $j_s = m$ such that $L_{j_p j_{p+1}} > 0$ for $1 \leq p \leq s-1$. Equation (B.2) implies that $\phi_{j_p} = \phi_{j_{p+1}}$ for $1 \leq p \leq s-1$. Hence, $\phi_1 = \phi_m$, another contradiction. We conclude that the right-hand side of (B.1) is positive, and thus that $(\lambda^*)'$ is also positive.

(c) A variational characterization of λ^* is given by

$$(B.3) \quad \lambda^* = \inf_{\sum_{j \in \Omega} \varphi_j^2 = 1} \left\{ \frac{d_I}{2} \sum_{j,k \in \Omega} L_{jk}(\varphi_j - \varphi_k)^2 + \sum_{j \in \Omega} (\gamma_j - \beta_j)\varphi_j^2 \right\},$$

and (3.7) is its corresponding Euler–Lagrange equation. Thus,

$$\lim_{d_I \rightarrow 0} \lambda^* = \inf_{\sum_{j \in \Omega} \varphi_j^2 = 1} \left\{ \sum_{j \in \Omega} (\gamma_j - \beta_j)\varphi_j^2 \right\}.$$

The right-hand side is minimized by setting $\varphi_j = 1$ for a single $j \in \Omega$ with the property that $\gamma_j - \beta_j = \min\{\gamma_k - \beta_k : k \in \Omega\}$ and letting $\varphi_j = 0$ otherwise.

- (d) Parts (b) and (c) show that λ^* is a strictly monotone increasing function of $d_I > 0$ that is bounded from below, and substituting $\phi_j = 1/\sqrt{n}$ for $j \in \Omega$ into (B.3) shows that λ^* is bounded from above. Therefore, λ^* has a limit $\lambda_\infty^* \in (\min\{\gamma_k - \beta_k : k \in \Omega\}, \infty)$ as $d_I \rightarrow \infty$. We divide both sides of (3.7) by d_I to get

$$(B.4) \quad \sum_{k \in \Omega} L_{jk}(\phi_k - \phi_j) + \frac{(\beta_j - \gamma_j)\phi_j}{d_I} + \frac{\lambda^* \phi_j}{d_I} = 0, \quad j \in \Omega.$$

Without loss of generality, we may assume that $\phi = (\phi_j)$ is a unit vector, i.e., $\sum_{j \in \Omega} \phi_j^2 = 1$. It follows from the positivity of ϕ and compactness that $\phi \rightarrow \bar{\phi}$, where $\bar{\phi}_j \geq 0$ for $j \in \Omega$ and $\sum_{j \in \Omega} \bar{\phi}_j^2 = 1$, for some positive sequence of values $d_I \rightarrow \infty$. Let this sequence be denoted by $d_I^{(l)}$. Taking such a limit in (B.4) produces

$$\sum_{k \in \Omega} L_{jk}(\bar{\phi}_k - \bar{\phi}_j) = 0, \quad j \in \Omega.$$

We can write this equation in matrix-vector form as $A\bar{\phi} = \bar{\phi}$, where $A = (L_{jk}/L_j)$. The nonnegativity and irreducibility of A implies that $\bar{\phi}$ is proportional to $(1, 1, \dots, 1)^t$, as both vectors belong to the principal eigenvalue $\mu = 1$. The fact that $\bar{\phi}$ is a nonnegative unit vector implies that $\bar{\phi}_j = 1/\sqrt{n}$ for $j \in \Omega$. Observe from the symmetry of L that $\sum_{j,k \in \Omega} L_{jk}(\phi_k - \phi_j) = 0$. Therefore, summing (3.7) with $d_I = d_I^{(l)}$ over all $j \in \Omega$ yields

$$(B.5) \quad \sum_{j \in \Omega} (\beta_j - \gamma_j)\phi_j + \lambda^*(d_I^{(l)}) \sum_{j \in \Omega} \phi_j = 0.$$

We let $d_I^{(l)} \rightarrow \infty$ to get

$$\sum_{j \in \Omega} (\beta_j - \gamma_j)\bar{\phi}_j + \lambda_\infty^* \sum_{j \in \Omega} \bar{\phi}_j = 0.$$

Since $\bar{\phi}_j = 1/\sqrt{n}$ for $j \in \Omega$, we obtain

$$\lambda_\infty^* = \frac{1}{n} \sum_{j \in \Omega} (\gamma_j - \beta_j) = \frac{\Sigma_\gamma - \Sigma_\beta}{n}.$$

Finally, parts (e) and (f) follow directly from parts (b), (c), and (d) together with the fact that H^+ is nonempty. \square

Appendix C.

Proof of Lemma 3.7.

- (a) We argue by induction on l for $I^{(l)}$. If $l = 0$, then the result is immediate because $I_j^{(0)} = \underline{I}_j = \epsilon\phi_j \in [0, 1]$ for $j \in \Omega$. Suppose now that $I_j^{(l)} \in [0, 1]$ for $0 \leq l \leq s$ and $j \in \Omega$, where $s \geq 0$, but that $I_m^{(s+1)} \notin [0, 1]$ for some $m \in \Omega$. Suppose first that $I_m^{(s+1)} < 0$. Without loss of generality, we may assume that $I_m^{(s+1)} = \min\{I_j^{(s+1)} : j \in \Omega\}$. Equation (3.11) with $l = s$ and $j = m$ implies that

$$-d_I \sum_{k \in \Omega} L_{mk}(I_k^{(s+1)} - I_m^{(s+1)}) + MI_m^{(s+1)} = [f_m(I_m^{(s)}) + M]I_m^{(s)}.$$

Since $I_m^{(s)} \in [0, 1]$, we have, by the properties of M ,

$$-d_I \sum_{k \in \Omega} L_{mk} (I_k^{(s+1)} - I_m^{(s+1)}) + MI_m^{(s+1)} \geq 0.$$

Since $MI_m^{(s+1)} < 0$, it follows that

$$d_I \sum_{k \in \Omega} L_{mk} (I_k^{(s+1)} - I_m^{(s+1)}) < 0.$$

However, this result contradicts the minimality of $I_m^{(s+1)}$. Suppose now that $I_m^{(s+1)} > 1$, and without loss of generality that $I_m^{(s+1)} = \max\{I_j^{(s+1)} : j \in \Omega\}$. Again, (3.11) with $l = s$ and $j = m$ implies that

$$-d_I \sum_{k \in \Omega} L_{mk} (I_k^{(s+1)} - I_m^{(s+1)}) + MI_m^{(s+1)} = F_m(I_m^{(s)}) + MI_m^{(s)}.$$

Since $I_m^{(s)} \in [0, 1]$, and $F_m(u) + Mu$ is a monotone increasing function of $u \in [0, 1]$, we have

$$F_m(I_m^{(s)}) + MI_m^{(s)} \leq F_m(1) + M \leq M,$$

where the last inequality follows from $F_m(1) = f_m(1) = -\gamma_m \leq 0$. Hence

$$-d_I \sum_{k \in \Omega} L_{mk} (I_k^{(s+1)} - I_m^{(s+1)}) + MI_m^{(s+1)} \leq M.$$

Since $I_m^{(s+1)} > 1$, we have

$$-d_I \sum_{k \in \Omega} L_{mk} (I_k^{(s+1)} - I_m^{(s+1)}) < 0.$$

However, this result contradicts the maximality of $I_m^{(s+1)}$. We conclude that $I_j^{(s+1)} \in [0, 1]$ for all $j \in \Omega$, and, by induction, $I_j^{(l)} \in [0, 1]$ for $l \geq 0$ and $j \in \Omega$. The argument for $I^{[l]}$ is similar.

- (b) We argue by induction for l for $\Delta I^{(l)}$. To show that $\Delta I^{(0)} \geq 0$, we suppose otherwise and obtain a contradiction. If $\Delta I^{(0)} \not\geq 0$, then there exists some $m \in \Omega$ such that $\Delta I_m^{(0)} < 0$. We may assume that $\Delta I_m^{(0)} = \min\{\Delta I_j^{(0)} : j \in \Omega\}$. Recall that ϵ was chosen so that $G(\underline{I}) = G(\epsilon\phi) \geq 0$. Equation (3.9) with $j = m$ and $I = I^{(0)} = \underline{I}$ implies that

$$G_m(I^{(0)}) = d_I \sum_{k \in \Omega} L_{mk} (I_k^{(0)} - I_m^{(0)}) + F_m(I_m^{(0)}) \geq 0.$$

It follows from this inequality and (3.11) with $l = 0$ and $j = m$ that

$$-d_I \sum_{k \in \Omega} L_{mk} (I_k^{(1)} - I_m^{(1)}) + MI_m^{(1)} \geq d_I \sum_{k \in \Omega} L_{mk} (I_m^{(0)} - I_k^{(0)}) + MI_m^{(0)}.$$

Therefore,

$$d_I \sum_{k \in \Omega} L_{mk} (\Delta I_k^{(0)} - \Delta I_m^{(0)}) \leq M \Delta I_m^{(0)} < 0.$$

However, this result contradicts the minimality of $\Delta I_m^{(0)}$. We conclude that $\Delta I^{(0)} \geq 0$.

Suppose now that $\Delta I^{(l)} \geq 0$ for $0 \leq l < s$, where $s \geq 0$, but that $\Delta I^{(s+1)} \not\geq 0$. Then there exists some $m \in \Omega$ such that $\Delta I_m^{(s+1)} < 0$. We may assume that $\Delta I_m^{(s+1)} = \min\{\Delta I_j^{(s+1)} : j \in \Omega\}$. We subtract (3.11) with $l = s$ and $j = m$ from (3.11) with $l = s + 1$ and $j = m$ to get

$$\begin{aligned} -d_I \sum_{k \in \Omega} L_{mk} (\Delta I_k^{(s+1)} - \Delta I_m^{(s+1)}) + M \Delta I_m^{(s+1)} \\ = F_m(I_m^{(s+1)}) - F_m(I_m^{(s)}) + M \Delta I_m^{(s)}. \end{aligned}$$

Recall from part (a) that $I_m^{(s)}$ and $I_m^{(s+1)}$ both lie within the interval $[0, 1]$. There exists ζ between $I_m^{(s)}$ and $I_m^{(s+1)}$ such that

$$-d_I \sum_{k \in \Omega} L_{mk} (\Delta I_k^{(s+1)} - \Delta I_m^{(s+1)}) + M \Delta I_m^{(s+1)} = [F'_m(\zeta) + M] \Delta I_m^{(s)}.$$

The right-hand side is nonnegative because $F'_m(\zeta) + M > 0$ and $\Delta I_m^{(s)} \geq 0$. Therefore,

$$d_I \sum_{k \in \Omega} L_{mk} (\Delta I_k^{(s+1)} - \Delta I_m^{(s+1)}) \leq M \Delta I_m^{(s+1)} < 0.$$

However, this result contradicts the minimality of $\Delta I_m^{(s+1)}$. We conclude that $\Delta I^{(s+1)} \geq 0$, and, by induction, $\Delta I^{(l)} \geq 0$ for $l \geq 0$. The arguments for $\Delta I^{[l]}$ and $\Delta I^{\{l\}}$ are similar, except that $\Delta I^{[1]} = I^{[1]} - I^{[0]} \leq 0$ by part (a) and $\Delta I^{\{0\}} = I^{[0]} - I^{(0)} \geq 0$ is immediately clear. \square

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